REMARKS

1. The Claim objections on claim 9 as well as claim 23 of the Office Action have been corrected as the examiner required.

2. The Office Action mentioned that "since many types of cells, other than MSC, have the ability to adhere to a tissue culture plate, it is unlikely that the cell culture device describe will only allow MSCs to adhere to the plate when a cell mixture other than bone marrow is uded." The applicant has made the remarks on previous amendment dated on September 19 2005. It has been well reported that MSCs are plastic-adherent cells, as stated in this published application [0007] "Friedenstein (Exp. Hematol. 4:276, 1976) placed whole bone marrow in culture plastic dishes and poured off the cells that were non-adherent after 4 hours. However, the isolated cells initially are heterogeneous and are difficult to clone." In section [0009], it also stated that "briefly, mesenchymal stem cells can be isolated with the use of a culture device depending on, for example, difference in cell size, different adherence capacity ... " Furthermore, section [0024] also disclosed that "by means of their characteristics of larger size (van Vlasselaer P, et al., supra), ease to adhere and their role in supporting haematopoietic stem cells." Moreover, the US patent 6,010,696 (filed on 07/1/1998) disclosed that "this process of removing the non-adherent cells during culture media changes results in purification of the mesenchymal stem cells which selectively adhere to the culture plates." (Column 4 lines 50~53) The US patent 6,576,465 also stated that "the cells adhere to tissue plastic or glass while bone accessory cells do not." (Column 11 lines 23~25) Actually, the MSCs are also called "plastic-adherent cells," which would be supported by many references, for example:

a) Colter DC, Class R, DiGirolamo CM, Prockop DJ. Rapid expansion of recycling

stem cells in cultures of plastic-adherent cells from human bone marrow. Proc Natl Acad Sci U S A. 2000 Mar 28;97(7):3213-8.

b) Phinney DG, Kopen G, Isaacson RL, Prockop DJ. Plastic adherent stromal cells from the bone marrow of commonly used strains of inbred mice: variations in yield, growth, and differentiation.
J Cell Biochem. 1999 Mar 15;72(4):570-85.

c) Gordon MY. Plastic-adherent cells in human bone marrow generate long-term hematopoiesis in vitro.Leukemia. 1994 May;8(5):865-70.

d) Gordon MY, Riley GP, Greaves MF.Plastic-adherent progenitor cells in human bone marrow. Exp Hematol. 1987 Aug;15(7):772-8.

3. The examiner also mentioned the "smallest circulating blood cell is 1.5μM as evidence by Burkitt et al.," and "the size of blood cells ranging from 1.5μM to 20μM." It has been disclosed in this specification that "after seeding bone marrow cells into the upper plate of the culture device which comprises pores with pore size ranging from about 0.4 to 40 microns in diameter therein, small-sized haematopoietic cells can pass through the pores in the plate to reach the plate base before adhering, and non-adherent cells can be removed by following changes of medium." [0029] The main purpose of the pore is to have the small-sized haematopoietic cells or blood cells to pass through. As indicated by the examiner , the skilled persons in the art would realize the sizes of haematopoietic cells or blood cells range from 1.5μM to 20μM. Therefore, the skilled persons in the art would realize to have the pore size ranging from 1.5μM to 20μM in order to have those cells passing through the pores in the plate to reach the plate base. Accordingly, the applicants have amended the pore sizes ranging from 1.5μM to 20μM. Furthermore, the blood cells as well as those other than MSCs will not

adhere on the plastic plates. Therefore, those cells other than MSCs will deform and pass through the pore size said about 1.5μM. In other words, it does not require to do "a large amount of experimentation" to determine the pore size of the culture device, as the Office Action mentioned.

4. This amendment with the pore size ranging from 1.5μM to 20μM does meet the description requirement, as the examiner pointed in the Office Action. Citing the In re Wertheim (CCPA 1976), the ranges described in the original specification included a range of 25%-60% and specific examples of 36% and 50 %. A limitation to between 35% and 60% did meet the description requirement. Furthermore, the size of blood cells, ranging from 1.5μM to 20μM as indicated by the examiner in prior art, certainly can lead those skilled in the art to make or use the invention.

5. The key point of the invention is "the mesenchymal stem cells retain and adhere onto the upper plate, and the other small-sized cells pass through the pores to the lower plate base." The MSC is usually larger in size and has the adherence property. Therefore, it will retain and adhere onto the upper plate. The other cells are usually smaller in size and do not have the adherence property. Therefore, they will pass through the pores to the lower plate base.

6. In sum, this application combining the characteristics of large size and plastic adherence can result in a "novel, simple, effective, and economic method of isolating MSCs." [0023] As mentioned previously, this application is not perfect, but it does help in the MSC recovering, as the application stated "In one preferred embodiment, cell populations having greater than 98% of human MSCs

can be obtained in accordance with the method of the invention, and such isolated MSCs can proliferate without differentiation and reach confluence even after 12 passages." [0011] This application is the first one to combine the two features together and to improve the isolation of MSCs. Accordingly, this application now should be placed in condition of allowance. An early Notice to this effect is respectfully expected.

Respectfully submitted:

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